REMARKS

I. Status of Claims:

Claims 24, 25 , 28, 31-38, and 42-45 remain under examination in this application, claims 1-6 and 13-23 having been withdrawn by the Examiner and claims 7-12, 26, 27, 29, 30, and 39-41 previously canceled. Claims 24 and 35 are amended herein. The claim amendments are supported by the application as filed, *e.g.,* at the paragraph bridging pages 26 and 27. No new matter is added.

II. Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description:

Claims 24, 25, 28, 31-38, and 42-45[1] are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement (*see,* Office Action at pages 3-5).

Although the Action concedes that the term "cytotoxic activity" as recited in the present claims reads on any effect on the cell that reduces cell growth or induces cell death, the Action maintains the written description rejection for two reasons. *First*, the Action states that Genestier *et al.*, *Blood*, 90(9): 3629-3639 (1997), in Table 2 and Figure 1 teach that different anti-HLA antibodies have different effects on cytotoxic activity and cellular proliferation (*see,* page 4, first full paragraph). *Second*, the Action purports that, because the specification of the present application defines minibody as an antibody that lacks a portion of a whole antibody, the broad genus of minibodies recited in the claims covers "hundreds if not thousands of possible antibody structures that are not a whole antibody" and Genestier allegedly teaches in Figure 4 that Fab' and F(ab')2 antibody fragments do not have increased cytotoxic activity compared to the full length antibody. The Action concludes that the written description requirement is not complied with, "given the data of Genestier, et al. which support not all HLA class I antibodies have cytotoxic activity and the instant disclosure does not characterize or identify the epitope or structure connected with the cytotoxic activity" (*see,* Office Action, sentence bridging pages 4-5). Applicants traverse.

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[1] The Action states that "claims 24, 25, 27-38, and 40-45" are rejected. Note, however, that claims 27, 29, 30, 40, and 41 were previously canceled.

With respect to the Action's argument that the present claims lack written description because Genestier teaches that different anti-HLA antibodies have different effects on cytotoxic activity and cellular proliferation, Applicants note that, while Genestier does teach that the antibodies that bind MHC class I differ in apoptosis activity and cellular proliferation activity, Genestier does not teach that any of the tested MHC class I antibodies lack one of those activities. The Genestier abstract states in relevant part:

> We show here that two MoAbs (mouse MoAb90 and rat YTH862) that bind to an epitope of the α1 domain of HLA class I heavy chain induce apoptotic cell death of activated, but not resting, peripheral T lymphocytes. **Other reference anti-HLA class I antibodies specific for distinct epitopes** of the α1 (B9.12.1), α2 (W6/32), or α3 (TP25.99) domains of the heavy chain **decreased T-cell proliferation** but had little or no apoptotic effect. (emphasis supplied).

In other words, all of the anti-HLA class I antibodies discussed by Genestier possess some activity that falls within the present application's definition of "cytotoxic."

The rejection appears also to stem from the Examiner's concern that the claim term "minibody" encompasses "hundreds if not thousands" of possible antibody structures, including Fab' and $F(ab')_2$ fragments (*see,* Office Action, page 4, second paragraph). Applicants direct the Examiner's attention to the limitation at the end of each of the independent claims (claims 24 and 35), which specifies that the minibody is an scFv or a diabody. Thus, the facts that the term "minibody" is broad and that Genestier *et al.* teach Fab' and $F(ab')_2$ fragments that do not have increased cytotoxic activity compared to the full length antibody are irrelevant to the question of whether the present claims meet the written description requirement. As previously noted in the response filed February 17, 2009, Genestier *et al.* if anything supports the sufficiency of Applicants' written description, as Genestier *et al.* discloses a genus of anti-HLA class I antibodies that are "cytotoxic" as defined in the present application. Furthermore, the present claims require that the antibody recognize either the α1 or α2 domain of an HLA-A antigen, *i.e.*, a well-characterized domain of a well-characterized antigen.

Applicants remind the Examiner that claims 24, 25, 28, and 31-34 are drawn to novel methods of producing and assaying an anti-HLA-A minibody, but do not require any given minibody assayed in the method to possess any activity other than the activity to bind to HLA-A. In contrast, claims 35-38 and 42-43 do require use of a minibody that has cytotoxic activity

greater than that of the whole antibody. According to Noelle v. Lederman, 355. F.3d 1343 (Fed. Cir. 2004), a claim drawn to an antibody that binds to a specified antigen has sufficient written description if the antigen is "well-characterized." It is indisputable that the α1 and α2 domains of HLA-A qualify as "well-characterized." In claims 35-38 and 42-42, Applicants are simply claiming a method that utilizes a scFv or diabody form of an anti-α1 or anti-α2 antibody, and confirming that the scFv or diabody has a cytotoxic activity greater than that of the parent antibody. Methods utilizing a scFv or diabody that does not have such activity will not fall within claim 35 or its dependents.

In view of the foregoing, Applicants submit that all of the concerns raised in the Action have been addressed. Applicants request reconsideration of this rejection and withdrawal of the same.

CONCLUSION

Applicants respectfully submit that the pending claims under examination are in condition for allowance. Accordingly, a timely Notice of Allowance is requested. If the Examiner would like to discuss any aspect of this case to move the prosecution of this case forward, she is invited to call the undersigned at the telephone number listed below.

Other than the RCE filing fee and the 3-month extension of time fee that are both being paid concurrently via the Electronic Filing System (EFS) by way of Deposit Account

authorization, no additional fees are believed to be due. Any other charges or credits may be applied to Deposit Account No. 06-1050, referencing Attorney Docket No. 14875-0141US1.

Respectfully submitted,

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